DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
5109 LEESBURG PIKE
FALLS CHURCH, VA 22041-3258

REPLY TO
ATTENTION OF

DASG-PPM-NC

10 SEP 2004

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: Medical Evaluation, Follow-Up, and Recording of Chemical Warfare (CW) Nerve Agent Casualties Outside of Storage, Demilitarization, and Research Settings

1. References. See Appendix A.

2. Exposure to chemical weapons is a continuing and significant risk to our deployed forces. This past May, two Soldiers were exposed to CW nerve agent from unexploded ordnance in Iraq. It is of paramount importance that our health care providers appropriately evaluate, manage, follow-up, report, and archive these cases.

3. Emergency medical management of chemical casualties is well established in our doctrine (see Appendix A). This memorandum supplements doctrine by establishing a procedure for medical evaluation and long term follow-up of these casualties. Our knowledge about these agents continues to expand; this guidance will ensure appropriate care for our personnel exposed to such agents.

4. The effects of CW nerve agent are summarized in Appendix B. Certain insecticides have equivalent effects and exposures are managed similarly. Clinical questions concerning the evaluation and management of these exposures should be addressed to the US Army Medical Research Institute of Chemical Defense (USAMRICD); their 24-hour contact information is listed in Appendix C.

5. The evaluation of nerve agent casualties includes obtaining Red Blood Cell Cholinesterase (RBC-ChE) levels whenever feasible, even in forward-deployed areas. This testing is critical to evaluating exposures and determining the safety of returning exposed individuals to duty. Guidance for interpretation of RBC-ChE results and for returning exposed persons to duty is contained in Appendices C and D, with a summary flow chart at Appendix E. Instructions for collection, handling, and shipment of clinical specimens are contained in Appendices F and G. In all cases, blood and urine specimens will be sent to USAMRICD for testing and archiving; if shipment of samples is not possible in forward-deployed locations, symptomatic patients should be evacuated for this purpose when the mission allows.

USAMRICD will send a portion of each sample to the Armed Forces Institute of Pathology for archiving.

6. Command Surgeons will report chemical casualty information, using the format in Appendix H, through command channels to the US Army Center for Health Promotion and Preventive Medicine (USACHPPM). Directions for reporting, recording, and archiving information related to nerve agent exposures is located in Appendix C. USACHPPM will maintain an archive of this information, and notify the Office of The Surgeon General (Current Operations) and the Deployment Health Clinical Center (DHCC).

7. Long-term annual follow-up of all confirmed exposures will be coordinated by the Deployment Health Clinical Center (DHCC) at Walter Reed Army Medical Center. Follow-up guidelines and DHCC's contact information is listed in Appendix C.

8. All primary care providers must become familiar with these guidelines. My point of contact for this memorandum is LTC John Rowe, Proponency Office for Preventive Medicine, john.rowe@otsg.amedd.army.mil, DSN 761-0022 or commercial (703) 681-0022.

FOR THE SURGEON GENERAL:

Encls (8)

JOSEPH G. WEBB, JR.
Major General
Deputy Surgeon General

DISTRIBUTION:
Commanders, MEDCOM Major Subordinate Commands
Commander, 18th MEDCOM
Director, National Guard Bureau, ATTN: Surgeon, 111 South George Mason Drive, Arlington, VA 22204-1382
Chief, U.S. Army Reserve Command, ATTN: Surgeon, 1401 Deshler Street, South West, Fort McPherson, GA 30330-2000
Commander, U.S. Army Training and Doctrine Command, ATTN: Surgeon, 7 Fenwick Road, Fort Monroe, VA 23651-5000
Commander, U.S. Army Forces Command, ATTN: Surgeon, Fort McPherson, GA 30330-6000
Commander, U.S. Army Materiel Command, ATTN: Surgeon, 5101 Eisenhower Avenue, Alexandria, VA 22333-0001

Commander, U.S. Army Test and Evaluation Command, ATTN: Surgeon, Park Center IV, 4501 Ford Avenue, Alexandria, VA 22333-0001
Commander, U.S. Army Special Operations Command, ATTN: Surgeon, Fort Bragg, NC 28307-5200
Commander, ARCENT, ATTN: Surgeon
Commander, US Army Pacific, ATTN: Surgeon
Commander, US Army South, ATTN: Surgeon
Commander, US Army Europe, ATTN: Surgeon
Director, DoD Deployment Health Clinical Center, Walter Reed Army Medical Center, Bldg. 2, Room 3G04, 6900 Georgia Avenue NW, Washington, D.C. 20307-5001
Director, Armed Forces Institute of Pathology, 6825 16th Street NW, Washington, DC 20306-6000

CC:
Commander, CJTF–HOA, ATTN: Surgeon
Commander, CFLCC, ATTN: Surgeon
Commander, MNC-I, ATTN: Surgeon
Commander, CJTF-76, ATTN: Surgeon
Commander, 3rd US Army, ATTN: Surgeon

Appendix A. References

1. Field Manual 8-285, Treatment of Chemical Casualties and Conventional Military Chemical Injuries, 22 Dec 95, http://www.army.mil/usapa/doctrine/8_Series_Collection_1.html.

2. Textbook of Military Medicine, Part I: Medical Aspects of Chemical and Biological Warfare, Office of The Surgeon General, 1997, http://www.bordeninstitute.army.mil/cwbw/default_index.htm.

3. Medical Management of Chemical Casualties Handbook, U.S. Army Medical Research Institute of Chemical Defense, 2000, http://ccc.apgea.army.mil.

4. Technical Guide 244, Medical NBC Battlebook, US Army Center for Health Promotion and Preventive Medicine (USACHPPM), July 99, http://ccc.apgea.army.mil.

5. Memorandum, MCM-0026-02, The Joint Chiefs of Staff (JCS), 29 Apr 02, Subject: Chemical Warfare (CW) Agent Exposure Planning Guidance.

6. Memorandum, MCM-0006-02, JCS, 1 Feb 02, Subject: Updated Procedures for Deployment Health Surveillance and Readiness.

7. Technical Bulletin - Medical 590, Red Blood Cell-Cholinesterase Testing and Quality Assurance, 30 Nov 01, http://chppm-www.apgea.army.mil/documents/TBMEDS/TBMED590.pdf.

8. Tri-service Reportable Medical Events, Guidelines and Case Definition Version 1.0, Army Medical Surveillance Activity, Jul 98. http://amsa.army.mil/documents/DoD_PDFs/Jul98TriServREGuide.pdf

9. Clinical Practice Guideline for Post-Deployment Health Evaluation and Management, Dec 01, http://www.pdhealth.mil/guidelines/default.asp.

10. Presidential Review Directive (PRD) 5, Planning for Health Preparedness for and Readjustment of the Military, Veterans, and Their Families After Future Deployments, Aug 98.

11. TB Med 296, Assay Techniques for Detection of Exposure to Sulfur Mustard, Cholinesterase Inhibitors, Sarin, Soman, GF, and Cyanide, May 96, http://chppm-www.apgea.army.mil/documents/TBMEDS/TB%20MED%20296.pdf.

12. Department of Defense Instruction (DoDI) 6490.3, Implementation and Application of Joint Medical Surveillance for Deployments, 7 Aug 97, http://www.dtic.mil/whs/directives/corres/pdf/i64903_080797/i64903p.pdf.

13. DoDI 6055.5, Industrial Hygiene and Occupational Health, with change 1, May 96. http://www.dtic.mil/whs/directives/corres/pdf/i60555wch1_011089/i60555p.pdf.

Appendix B. Summary of Nerve Agent Effects

Type of Agent	Effects	Onset Time	Immediate Care
Nerve (GA, GB, GD, VX)	VAPOR: *Mild*: Small pupil (miosis), rhinorrhea, shortness of breath; tightness of chest; headache, eye pain *Severe*: Vomiting, convulsions, apnea; flaccid paralysis; LIQUID: Headache, miosis. Muscular twitching, sweating at site, GI effects; weakness; *Severe*: Vomiting, convulsions, apnea; flaccid paralysis;	VAPOR: seconds to minutes LIQUID: minutes to 18 hours	Ventilation as needed Atropine; 2-PAMCl If severe- diazepam

References: *Medical NBC Battlebook*, USACHPPM TG 2444, July 1999; and *Management of Chemical Warfare Agent Casualties*, F. Sidell, 1995.

Appendix C. Instructions for Medical Evaluation, Follow-Up, and Recording of Nerve Agent Casualties Outside of Storage, Demilitarization, and Research Settings

C-1. Purpose. This guidance establishes procedures to evaluate and treat individuals exposed to chemical warfare (CW) nerve agents or organophosphorous pesticides during deployment and combat operations. It identifies specific procedures that the Department of the Army will use to employ clinical evaluation procedures, identifies follow-up and disposition policies, establishes a clinical specimen archive, and establishes requirements for submission of reports so that information related to such exposures may be archived by way of an Occupational and Environmental Health Incident Report at the United States Army Center for Health Promotion and Preventive Medicine (USACHPPM).

C-2. Applicability. This guidance applies to all Department of Army personnel, including government civilian employees, contractors, and volunteers accompanying US forces.

C-3. Guidelines.

a. Initial Medical Evaluation and Treatment. The care of personnel potentially exposed to CW nerve agents is in accordance with references 1 through 4 in Appendix A, supplemented by consultation with the US Army Medical Research Institute of Chemical Defense as needed (see paragraph C-3.k.).

b. Laboratory Testing. Red Blood Cell Cholinesterase (RBC-ChE) testing will be conducted on all individuals exhibiting signs and symptoms compatible with nerve agent exposure, or for those individuals who are determined to be potentially exposed. An individual is considered potentially exposed if either there is: (a) a positive nerve agent detection as a result of an automated test/alarm, a positive hand held field test, or as a result of other approved sampling and analysis judged to be accurate and performed in accordance with Service guidelines indicating possible presence of a nerve agent; (b) when intelligence or other operational reporting or a commander determines that nerve agent exposures may have occurred; or (c) when an individual exhibits signs and/or symptoms consistent with nerve agent exposure.

(1) A blood sample for RBC-ChE should be obtained as soon as possible after the exposure, and then weekly until no further increase is noted for three consecutive weeks, which may take up to 90 days (see below). If the exposed individual has a baseline RBC-ChE established as part of an occupational health program (see related reference, DA Pam 40-8), post-exposure weekly testing can be discontinued when those levels return to the original baseline. A depression greater than 10% from baseline RBC-ChE levels could represent an exposure to nerve agent or anticholinesterase pesticide without obvious symptoms. However, local signs and symptoms in the eye, nose, and airways caused by small amounts of vapor are due to direct effects of the vapor on the organ; no correlation between the severity of these effects and the RBC-ChE activity appears to exist.

(2) The preferred method of RBC-ChE analysis is the Manual 17-Minute Change in pH Method. However, this is generally not available in a theater of operations. If possible, the separated red blood cells should be shipped refrigerated (placed on ice; maintained at 2-8 degrees Celsius) to the USACHPPM Cholinesterase Reference Lab (CRL), located at Aberdeen Proving Ground, MD, to arrive within 14 days of the date drawn. Complete instructions on collection, handling, and shipping of blood specimens for RBC-ChE testing at the CRL are included in Appendix G.

(3) When shipping refrigerated blood samples to USACHPPM within 14 days is not practical, an alternative method of RBC-ChE testing acceptable to the Cholinesterase Reference Laboratory at USACHPPM should be used. One such method is the spectrophotometric assay. A conversion factor has been developed by the Cholinesterase Reference Laboratory to compare results from the two different methods, however it is best to use the same method previously used on a particular patient so that more accurate comparisons can be made. The spectrophotometric assay automatically adjusts for hemoglobin concentration.

(4) An additional blood specimen (lavender-top tube) should be taken during the first blood draw and placed on ice (2-8 degrees Celsius; not frozen) and sent to the US Army Medical Research Institute of Chemical Defense (USAMRICD). The USAMRICD will split the sample and send it to the Armed Forces Institute of Pathology (AFIP) for archiving in the CW Agent Registry for possible future analysis. Addresses for shipment and shipping instructions are listed at Appendix F. If cholinesterase testing is done in theater, this does not eliminate the need to ship a specimen to USAMRICD for analysis and archiving at AFIP, as noted above. When shipping specimens to USAMRICD is not possible, symptomatic patients should be evacuated for this purpose, as the tactical situation permits.

(5) A urine specimen should be collected as soon as possible after exposure, frozen, and transported to USAMRICD in accordance with Appendix F. USAMRICD will also send a portion of the urine sample for archiving at AFIP. When shipping specimens to USAMRICD is not possible, symptomatic patients should be evacuated for this purpose, as the tactical situation permits.

(6) Complete guidelines for the collecting, handling, and shipping of blood and urine from patients exposed to nerve agents are located in Appendix F. Instructions for collecting and shipping to all types of chemical warfare agents are located at http://ccc.apgea.army.mil, or http://chemdef.apgea.army.mil. Ensure clinical information, including last known exposure to pyridostigmine bromide (PB) or other medications that might affect cholinesterase testing, accompanies the specimens as outlined in Appendices F and H. RBC-ChE laboratory procedures and quality assurance are outlined in TB Med 590, reference 7, http://chppm-www.apgea.army.mil.

c. Guidelines for Return to Duty.

(1) Tactical situation permitting, an individual should not return to duty where repeated exposure to cholinesterase-inhibiting substances is possible, until the RBC-ChE activity has returned to 90% or more of the individual's baseline RBC-ChE activity

and the person is asymptomatic for at least one week. Individuals without baselines established can be safely returned to duty after three consecutive weekly tests show no further increase in RBC-ChE activity (and the individual is asymptomatic); this can be interpreted as the individual's baseline. This is a conservative approach which should be taken if a reasonable potential for additional exposure exists for the same individual due to mission or duty.

(2) An individual may be returned to duty where exposure to anticholinesterase substances is unlikely when it is supported by clinical assessment, even without the 90% recovery of baseline cholinesterase activity (or when a non-baselined individual's RBC-ChE activity continues to climb on weekly testing). Attention should be given to ensure miosis (pinpoint pupils) do not endanger or interfere with the work required. Visual acuity must be compared with visual demands of the job, and mental status must be compatible with the demands of the job.

d. Guidelines for Medical Evacuation. Evacuation of nerve agent casualties out of theater for definitive evaluation and follow-up, usually at a Regional Medical Center, should be conducted for casualties severe enough to require the administration of three or more Nerve Agent Antidote (MARK I) kits, casualties with a loss of consciousness or seizures, casualties with documented mental status changes, or casualties with neurobehavioral complaints whose duration exceeds the theater holding capacity (or 3-4 weeks) or who cannot be evaluated in theater. This last category of neurobehavioral complaints may represent a post-exposure syndrome which usually lasts less than eight weeks and then resolves. This syndrome is not associated with all exposures and is not necessarily related to severity of exposure. The symptoms can include headache, insomnia, nightmares, depression, lethargy, etc. Supportive medications are prescribed for pain, sleep, depression, etc.

e. Definitive Medical Evaluation for Medically Evacuated Nerve Agent Casualties.

(1) Medically evacuated soldiers should have a thorough physical examination documented, to include neurological examination on admission. Electroencephalogram (EEG) should be performed on admission. Serial evaluations focusing on any abnormalities should be performed until resolution with time and appropriate treatment. RBC-ChE levels should be followed weekly until return to baseline or stable for 3 consecutive weeks.

(2) Consideration may be given to performing additional studies such as a sleep study, functional MRI, and psychological evaluations for acute stress reaction. Anticholinesterase agents can disrupt sleep and mood regulation; therefore it may be difficult to distinguish the consequences of nerve agent exposure from stress reaction. Proper mental health care which emphasizes the expectation of successful recovery and full return to duty should be included in the care plan.

f. Long Term Follow-Up Evaluation for All Nerve Agent Casualties.

(1) All organophosphate-poisoned casualties (not just those requiring medical evacuation) will undergo long term follow-up evaluation by their primary care provider as

described below. This will be accomplished in coordination with the DoD Deployment Health Clinical Center (DHCC); contact information is listed below.

(2) One year after full convalescence, anticholinesterase-exposed patients should undergo a thorough follow-up assessment by their primary care provider, including, at a minimum, a careful physical examination with attention to subtle neurological deficits, and a repeat of screening laboratory studies including RBC-ChE (by same technique). If any studies, such as EEG, were ever abnormal post exposure, repeat those studies.

(3) If any studies related to nerve agent exposure prove to be abnormal at one-year follow-up, treat appropriately, and follow-up annually (or more frequently, as indicated) with appropriate physical examination and studies until there is clear evidence a problem no longer exists.

(4) Once a patient has no nerve agent-related symptoms and has had normal studies at annual follow-up, the patient should be followed annually with a medical history and directed physical examination (toward any new-onset symptoms) coordinated by the DHCC.

(5) Patients having questions or needing annual follow-up can contact the DHCC at (800) 796-9699, e-mail pdhealth@amedd.army.mil, or visit their web site at http://www.pdhealth.mil/.

g. Medical Records Documentation.

(1) Nerve agent exposed persons who have been evaluated/treated by medical personnel must have this evaluation/treatment documented in their individual medical records. This includes documentation of International Classification of Diseases, 9th Edition (ICD-9), category 989, "Toxic effect of other substances, chiefly nonmedicinal as to source" reportable events due to clinically observed CW agent effects as well as notation of any negative findings when medical evaluation indicates that an individual was likely not exposed to chemical agent. This must also include documentation of any treatments/antidotes given. Command Surgeons should ensure that all potentially exposed persons receive appropriate medical evaluation/treatment.

(2) Laboratory assays such as RBC-ChE, plasma (butyryl-) ChE, etc., are not required for the ICD-9 989, case definition, which defines chemical agent exposures based on clinical observation of signs compatible with agent exposures such as those described in Appendix B. The use of laboratory assays for these agents in the field environment has limitations, and even when used successfully is not an indication of adverse health effects, but only an indication of exposure. Results of any such tests should be documented in the individual's medical record.

h. Reporting and Archiving of Potential Nerve Agent Exposures.

(1) JCS memoranda MCM-0026-02 and MCM-0006-02 (references 5 and 6, respectively) establish the requirement to ensure that deployment health surveillance

and readiness documentation requirements are met following a suspected or actual CW incident. This documentation includes identifying information for individuals that are exposed or possibly exposed to CW agent (protected or unprotected) their location, time, hazard area, and all monitoring results (to include those within standards).

(2) The treating physician will report potential chemical agent exposures through command channels. The Command Surgeon will obtain the following information and report it, using the format located in Appendix H, through command channels to USACHPPM as described below.

(a) All theater area NBC reports (initial and follow on, i.e., NBC 1,2,3,4,5,6), situation reports (SITREPS), and related confirmatory data (from NBCWRS/ G3/OPS-NBC). At a minimum data must include unit, location, date/time group of incident, type of CW event suspected/confirmed, and sampling type and location if available.

(b) All unit personnel data and personal identifiers; name, rank, SSN, and unit identification (Unit Identification Code, if known).

(c) All CW agent-related casualty treatment. This includes ICD-9 989 reportable events based on clinically observed CW agent health effects, whether or not treatment was provided. Medical personnel must also document any negative findings in individual records when medical evaluation identifies no physical findings supportive of chemical agent exposure.

(3) Command Surgeons will evaluate and compile data and perform initial assessments of units/personnel potentially exposed or at risk and forward copies of data (both field detector data and confirmatory laboratory data), as well as data summaries, final reports, and investigations related to CW agent events through command channels to USACHPPM – contact information is below. USACHPPM will archive a report based on data provided. Contact information for USACHPPM is as follows:

US Army Center For Health Promotion and Preventive Medicine
ATTN: MCHB-TS-RDE
5158 Blackhawk Road
Aberdeen Proving Grounds, MD 21010-5422
1-800-222-9698, DSN 584-6096; or commercial (410) 436-6096
Secure DSN 584- or commercial 410-436-4244
Secure email: OEHdata@usachppm.smil.mil
Secure web server: usachppm1.army.smil.mil

(4) The USACHPPM will acknowledge receipt of these reports to the Office of The Surgeon General, ATTN: Current Operations (703-681-8052, DSN 761, OPNS@otsg.amedd.army.mil). USACHPPM will also forward the information to the Deployment Health Clinical Center at Walter Reed Army Medical Center. USACHPPM maintains information on all types of deployment-related exposures in the Deployment Environmental Surveillance Program (DESP), the designated DoD data repository for all deployment-related occupational and environmental health surveillance data. The

DESP will coordinate with the Army Medical Surveillance Activity to ensure that all medical data is coordinated and archived in the Deployment Medical Surveillance System (DMSS), the designated DoD data repository for all medical surveillance data.

(5) The AFIP will maintain an archive of serum and RBC samples from all suspected CW exposed cases. The archive will be maintained under the CW Agent Registry.

i. Health Risk Communication. The physician or other medical provider will inform each potentially exposed patient of the clinical impression and the purpose of any laboratory or other evaluation or treatment procedures and of any results when they become available. Health risks associated with the intensity and duration of exposure and with the degree of signs/symptoms will be communicated to the individuals. All laboratory results will be entered into the individual medical records. Health care providers are encouraged to use the resources listed in Appendix A, and to contact the USAMRICD when questions arise, at (410) 436-2230 /4484 /3276.

j. Post-Deployment Health Assessments (DD Form 2796). When the DD Form 2796 is completed, the appropriate health care provider will follow-up on the mention of any potential nerve agent exposure. Personnel may be referred for further medical evaluations in accordance with redeployment clinical practice guidelines and this memorandum. The DD Form 2796 will be annotated and documented in the medical records. If needed, a follow-up specimen establishing a "retrospective" baseline RBC-ChE level may be obtained after at least 90 days post-exposure.

k. Consultative Services and Further Information. Training in the medical management of nerve agent casualties may be obtained from the Medical Management of Chemical and Biological Casualties Course, 6H-F26/877,879 or the Field Management of Chemical and Biological Casualties Course, 6H-F27/322-F27. These courses are offered by the USAMRICD. The USAMRICD Chemical Casualty Care website, http://ccc.apgea.army.mil contains further information. Contact the USAMRICD Chemical Casualty Care Division for consultation at their office (410) 436-2230 /4484/3276, cell phone (410) 322-6808, or e-mail ccc@apg.amedd.army.mil.

Appendix D. Interpretation of RBC-ChE Results

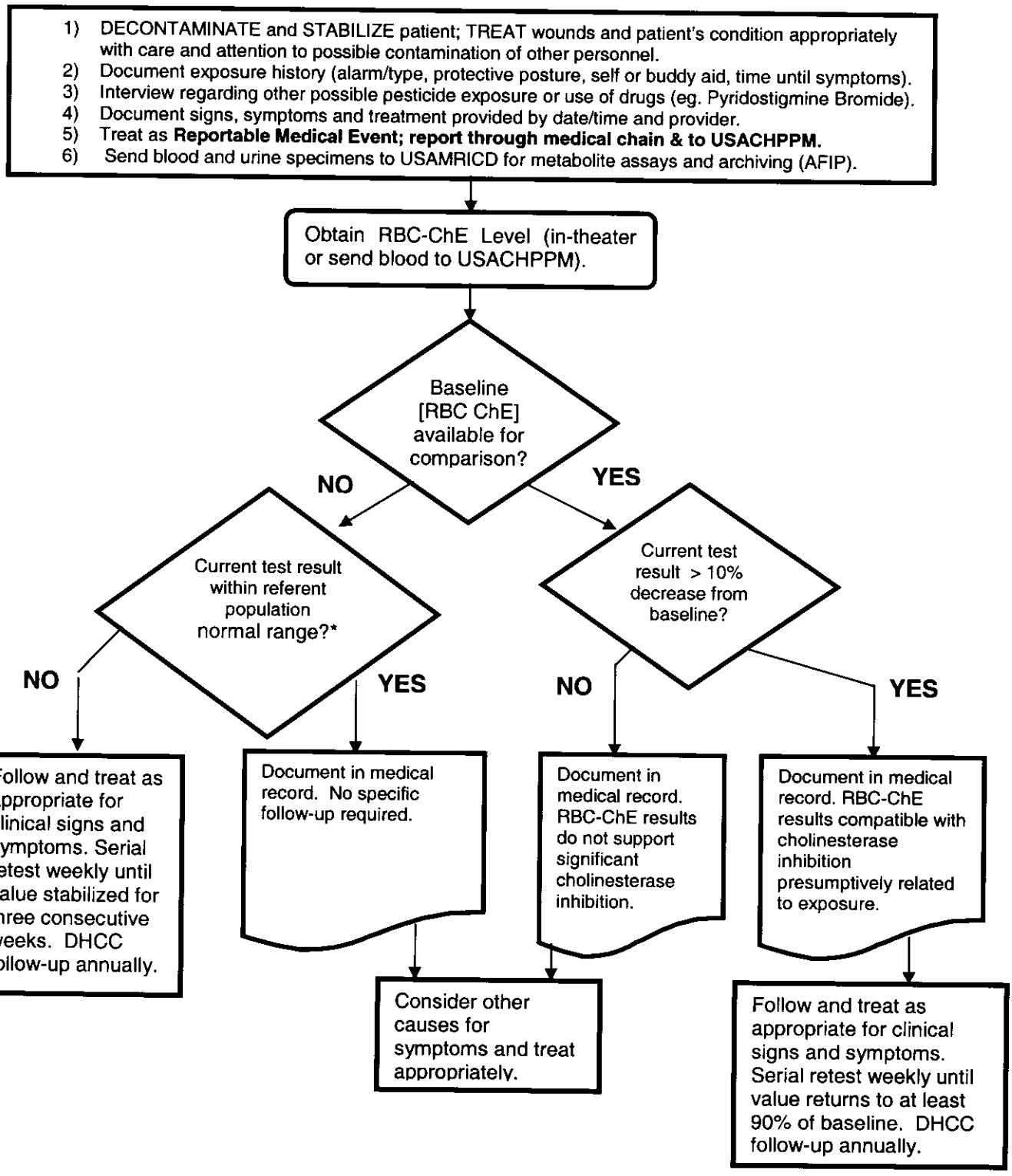
The inhibition of red blood cell cholinesterase (RBC-ChE) is a commonly used biological marker for identifying exposure to organophosphorous compounds – this includes a variety of pesticides as well as the CW nerve agents. Additionally, pyridostigmine bromide (PB) depresses cholinesterase activity. RBC-ChE testing is used for screening personnel for possible exposure to anti-cholinergic compounds. Positive results should be followed-up with a more definitive test to specifically identify which compound(s) were responsible for the inhibition of cholinesterase. RBC-ChE determinations are useful in three situations: (1) to identify unrecognized organophosphate exposures, (2) to document known or suspected organophosphate exposures or lack of significant systemic exposures, and (3) to assist in the determining when it is safe to return a worker to duty where additional exposure to cholinesterase inhibiting substances is possible.

For the most meaningful results, the test should be conducted as soon as possible after exposure and compared with an individual's "baseline" RBC-ChE level. Unless an antidote is given, RBC-ChE will remain irreversibly inhibited and activity will return as new RBCs are produced (about 1% per day). Thus, depending upon the severity of the nerve agent exposure, a depression in RBC-ChE levels may be detectable for 1-3 months. Depressions of greater than 10% from an established baseline level are indicative of a potential exposure. Some exposures, particularly vapor only, may not be associated with cholinesterase depression, and such depression in and of itself has not been associated with any physiological effect – acute or delayed. Because there is substantial human variability, both in baseline levels as well as in response to exposure, the results will have limited meaning with regard to an individual's exposure without comparison baseline data. For this reason, it is beneficial to perform baseline RBC-ChE testing prior to deployment for certain high-risk individuals, such as those involved in the destruction of explosive devices.

If no baseline is identified for an individual potentially exposed to nerve agent, results would be compared to the lower value population norm (0.62 delta pH units). Further RBC-ChE tests would be followed weekly until their values have stabilized for three consecutive weeks, which would be considered a return to baseline. Recovery from cholinesterase depression could take as long as 90 days, depending on the degree of depression. At a minimum, any individual with a depression of greater than 10% from their baseline, or a result below the population norm without baseline must have a follow-up test after an exposure-free period of at least 90 but no greater than 120 days, documented in their medical record to establish return to baseline.

The RBC-ChE baselines may fluctuate in some individuals monitored over a period of time. This fluctuation reflects the natural physiological enzyme variance in humans. As noted previously, exposure to pesticides, pyridostigmine bromide (PB), and other substances with anticholinesterase activity (besides nerve agent) can also depress RBC-ChE levels, and should be considered in all situations. Cholinesterase depressions associated with PB, which is a carbamate, a reversible inhibitor of RBC-ChE, will be readily apparent on serial assays, as PB dissociates from the enzyme causing the enzyme activity to rebound much more rapidly than with nerve agents.

Appendix E. Use of Red Blood Cell Cholinesterase Level (RBC-ChE) in Suspected Nerve Agent Exposure



* The lower level population norm for the Delta pH method is 0.62 delta pH units. Using the baseline as the "100%" value, a decrease of 10% or more of an individual's baseline is compatible with cholinesterase inhibition presumptively related to exposure.

Appendix F. Sample Collection, Handling, and Shipment: Excerpt From the US Army Medical Research Institute for Chemical Defense (USAMRICD) Standing Operating Procedure for Obtaining, Handling, and Shipping Biomedical Samples

IMPORTANT

THIS DOCUMENT WILL BE PERIODICALLY UPDATED. PLEASE ROUTINELY CONSULT THE CHEMICAL CASUALTY CARE WEBSITE (http://ccc.apgea.army.mil) OR US ARMY MEDICAL RESEARCH INSTITUTE OF CHEMICAL DEFENSE PERSONNEL FOR THE MOST CURRENT PROCEDURES

F-1. Purpose and Applicability

Assay techniques for detection of chemical warfare agents in biomedical samples are described in TB MED 296. The purpose of this document is to provide information on procedures for obtaining, handling, and shipment of biomedical samples for analysis as described in TB MED 296 at the US Army Medical Research Institute of Chemical Defense (USAMRICD). **Note that analytical methodologies utilized for sample analysis are for forensic investigational purposes only. They are not Food and Drug Administration-approved clinical procedures are not intended to provide the physician with information to implement or modify treatment.** The procedures apply only to the detection of chemical agents in biomedical fluids.

F-2. Nerve Agents

A. Samples to be Collected:

1. Blood Sample – Mandatory: The analysis of acetylcholinesterase activity in blood is the primary method used to screen for possible exposure to nerve agents. This is accomplished in-theater or at USACHPPM's Cholinesterase Reference Lab. A blood sample is also needed by USAMRICD for analysis and archival purposes. USAMRICD will split the sample and send a portion to the Armed Forces Institute of Pathology (AFIP) for archiving and possible future analysis. Blood should be obtained according to the procedures outlined in paragraph F-3.B., Blood Sample Collection.

2. Urine Sample – Mandatory: The collection of urine is mandatory for archival purposes and for detecting the presence of hydrolysis compounds to nerve agents. USAMRICD will split the sample and send a portion to AFIP for archiving. The analysis of urine samples can be used for definitive identification of the parent agent following a suspected exposure. Urine should be obtained according to the procedures outlined in paragraph F-3.C., Urine Sample Collection.

F-3. Collection of Samples: The collection of all biomedical samples should be done under close supervision of a qualified health care provider or physician to prevent contamination, tampering, or mislabeling. A tamper-proof strip should be placed across the container and clearly marked/identified with the patient's name, social security

number, and date, with the patient's initials. A chain-of-custody form (DD Form 1911) should be initiated at the time the samples are generated.

A. Biomedical Sample Collection Kit: A list of items necessary for collection of samples can be found below in paragraph F-6., Biomedical Sample Collection Kit. Most materials are readily available from medical units. If materials cannot be obtained, contact the USAMRICD (see paragraph F-4.B., Contact Information), and a Biomedical Sample Collection Kit can be shipped. NOTE: Shipment can only be made to authorized Military Health Care Providers.

B. Blood Sample Collection: It is recommended that the samples be cautiously handled from the start of the collection to maintain integrity and preclude the possibility of contamination, tampering, or mislabeling. All samples should be collected under the close supervision of a health care provider/physician as soon as possible following the suspected exposure.

1. Minimum Volume: At least 2 ml of blood are required for analysis.

2. Anticoagulant: Blood should be drawn into Vacutainers (purple top tubes) containing ethylenediaminetetraacetic acid (EDTA) as an anticoagulant.

3. Shipping Method: Blood samples should be kept refrigerated (not frozen) and shipped with adequate ice packs to maintain samples as cold as possible without freezing. If immediate shipping is not possible, the blood sample should be stored refrigerated.

4. Documents to be Included with the Package:

a. Incident Report Form (Appendix H)

b. DD Form 1911 – Chain of Custody (page F-6)

C. Urine Sample Collection: Urine samples should be taken to confirm suspected exposure to nerve agent. The collection of urine samples should be done under the close supervision of a health care provider and care should be taken to ensure appropriate handling so as to minimize chances for contamination from the environment or handling personnel. The urine should be collected immediately following suspected exposure or at the earliest possible time. Urine should be collected in clean urine cups. Immediately transfer 10-30 milliliters (ml) of the urine to a plastic sample/tube container.

1. Minimum Volume: At least 10-30 ml of urine are required.

2. Shipping Method: All urine samples should be shipped with dry ice in order that they remain frozen.

3. Documents to be Included with the Package:

a. Incident Report Form (Appendix H)

b. DD Form 1911 (Materiel Courier Report) – Chain of Custody (page F-6)

4. Special Considerations: Permit enough air space in the container to allow for sample expansion during freezing. Sample containers made of non-breakable plastic, which can withstand cryogenic temperatures, should be used during shipping.

F-4. Shipping of Samples: Approval must be obtained prior to shipment of samples. Authorization can be obtained by phone or E-mail using the contact information noted below. All urine samples in sealed containers should be shipped in dry ice in order that they remain frozen. Blood should be shipped with ice packs and be maintained as cold as possible without freezing. If immediate shipping is not possible, samples of urine should be stored frozen and blood, refrigerated. Shipment should be made as expeditiously as possible to maintain temperature control of the samples.

A. Ship to:

Commander
US Army Medical Research Institute of Chemical Defense
ATTN: MCMR-UV-PA/Analytical Chemistry
3100 Ricketts Point Road
Aberdeen Proving Ground, MD 21010-5400

B. Contact Information:

Duty Hours: 0730-1630, Monday-Friday
Phone: 410-436-4254 or 410-436-2173
E-mail: mricdbiosamples@APG.AMEDD.ARMY.MIL

Off-duty Hours: Staff Duty Officer (SDO), cell phone 410-322-6822.

C. Documents to be Included with the Shipping Package

1. Incident Report Form: A blank Incident Report Form is provided at Appendix H. Enclose the information requested on this form in the shipping package, inserted inside of a plastic bag to protect from moisture.

2. DD Form 1911, Materiel Courier Receipt: The DD Form 1911 (page F-6) is a chain of custody form that should be initiated at the sample collection point and accompany the samples. An example of how to fill out the DD Form 1911 is provided on page F-7.

F-5. Sample Analysis: Turn-Around Time (From Receipt of Sample at USAMRICD)

TEST	SAMPLE	TURN-AROUND TIME[1]
Cholinesterase Inhibition (AChE), BuChE)	Blood	24-48 hours
Nerve Agent Hydrolysis Products (GB, GD, GF)	Urine[2], Blood	72 hours

[1]Results of any assays performed at USAMRICD will be reported back to the requesting physician and to the Deployment Environmental Surveillance Program at USACHPPM. The requesting physician is responsible for ensuring the results are recorded in the individual medical record.

[2]Urine samples are the primary specimen needed for the Nerve Agent Hydrolysis Product assays.

F-6. Biomedical Sample Collection Kit (packing list) for CW Verification

Item	Unit	Quantity
Urine Collection:		
urine collection containers w/lids	ea	5
15 ml conical tube, plastic Sarstedt #62.554.002	ea	5
plastic transfer pippette	ea	10
Blood Collection:		
Vacutainer Tubes w/EDTA, 10ml, Becton Dickinson #366457	ea	5
Misc.		
nitrile exam gloves, medium, Safeskin #57067	pr	1
tamperproof seals	ea	10
storage/packaging/shipping container	ea	1
ColdPacks	ea	2
plastic bags	ea	5
Documents:		
Sample Collection SOP	ea	1
Chain of Custody Form (DD1911) Blank	ea	2
Chain of Custody Form (DD1911) Example	ea	1
Incident Report Form	ea	2
USAMRICD shipping label	ea	2

MATERIEL COURIER RECEIPT

SHIPPER'S CONTROL/DOCUMENT NO.

SHIPPER — SUPPLY ACCOUNT NUMBER

DESTINATION — SUPPLY ACCOUNT NUMBER

I certify by my signature that I have received the materiel listed on this form and am aware of the applicable safety and security requirements.

SHIPMENT TRANSFERS

FIRST	LOCATION OF TRANSFER	DATE (YR/MO/DAY)
	RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.)	ORGAN. OR ACCOUNT NO.
	SIGNATURE	SOCIAL SECURITY NUMBER
SECOND	LOCATION OF TRANSFER	DATE (YR/MO/DAY)
	RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.)	ORGAN. OR ACCOUNT NO.
	SIGNATURE	SOCIAL SECURITY NUMBER
THIRD	LOCATION OF TRANSFER	DATE (YR/MO/DAY)
	RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.)	ORGAN. OR ACCOUNT NO.
	SIGNATURE	SOCIAL SECURITY NUMBER
FOURTH	LOCATION OF TRANSFER	DATE (YR/MO/DAY)
	RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.)	ORGAN. OR ACCOUNT NO.
	SIGNATURE	SOCIAL SECURITY NUMBER
FIFTH	LOCATION OF TRANSFER	DATE (YR/MO/DAY)
	RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.)	ORGAN. OR ACCOUNT NO.
	SIGNATURE	SOCIAL SECURITY NUMBER

PRIVACY ACT STATEMENT

AUTHORITY 5 U.S.C., Sec 552a (PL 93-579)
PRINCIPLE PURPOSES: To provide a receipt for transfer of controlled materiel. The use of the SSAN is required and is necessary to provide positive identification of the individuals receipting for the materiel.
ROUTINE USES: To document transfer of materiel from a shipper to a courier, courier to courier and/ or receiver.
DISCLOSURE IS VOLUNTARY: Since the SSAN must be used, refusal to provide SSAN may be grounds for action to remove the individual concerned from duties involving the materiel transferred by use of this form.

SHIPMENT DESCRIPTION

LINE NUMBER	QUANTITY	SERIAL NUMBERS	REMARKS

DD FORM 1911, MAY 82 — PREVIOUS EDITION MAY BE USED UNTIL 31 DEC 82. — USAPPC V1.01

MATERIEL COURIER RECEIPT

SHIPPER'S CONTROL/DOCUMENT NO

SHIPPER: Umatilla Health Clinic, Oregon — SUPPLY ACCOUNT NUMBER

DESTINATION: USAMRICD APG, MD — SUPPLY ACCOUNT NUMBER

I certify by my signature that I have received the material listed on this form and am aware of the applicable safety and security requirements

PRIVACY ACT STATEMENT

AUTHORITY 5 U.S.C. Sec 552a (PL 93-579)
PRINCIPLE PURPOSES: To provide a receipt for transfer of controlled material. The use of the SSAN is required and is necessary to provide positive identification of the individuals receipting for the material.
ROUTINE USES: To document transfer of material from a shipper to a courier, courier to courier and/or receiver.
DISCLOSURE IS VOLUNTARY. Since the SSAN must be used, refusal to provide SSAN may be grounds for action to remove the individual concerned from duties involving the material transferred by use of this form.

SHIPMENT TRANSFERS

	LOCATION OF TRANSFER	DATE (YYMMDDAY)
FIRST	Umatilla Health Clinic, Umatilla, OR	03/01/31

RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.): Doe, Jane W — ORGAN OR ACCOUNT NO:

SIGNATURE: *Jane W. Doe* — SOCIAL SECURITY NUMBER: 123-45-6789

	LOCATION OF TRANSFER	DATE (YYMMDDAY)
SECOND	USAMRICD, Bldg E3100, Rm 39, APG, MD 21010-5400	03/01/31

RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.): Smith, John A. — ORGAN OR ACCOUNT NO:

SIGNATURE: *John A. Smith* — SOCIAL SECURITY NUMBER: 987-65-4321

	LOCATION OF TRANSFER	DATE (YYMMDDAY)
THIRD		

RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.): — ORGAN OR ACCOUNT NO:

SIGNATURE: — SOCIAL SECURITY NUMBER:

	LOCATION OF TRANSFER	DATE (YYMMDDAY)
FOURTH		

RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.): — ORGAN OR ACCOUNT NO:

SIGNATURE: — SOCIAL SECURITY NUMBER:

	LOCATION OF TRANSFER	DATE (YYMMDDAY)
FIFTH		

RECIPIENT'S PRINTED NAME (LAST, FIRST, M.I.): — ORGAN OR ACCOUNT NO:

SIGNATURE: — SOCIAL SECURITY NUMBER:

SHIPMENT DESCRIPTION

LINE NUMBER	QUANTITY	SERIAL NUMBERS	REMARKS
1	2	Urine Specimens (Frozen)	
2	3	Blood Specimens (Unfrozen)	
		transfer to USAMRICD	
			Received samples at MRICD at 1225. Specimens were contained within a shipping cooler with KoolPacks. Samples were removed from cooler and visually inspected. Blood specimens (unfrozen) ~~were placed in refrigerator, urine specimens (frozen) were placed in~~ –70 C freezer. All seals intact. Room 39 door locked and secured.

DD FORM 1911, MAY 82 — PREVIOUS EDITION MAY BE USED UNTIL 31 DEC 82 — USAPPC V1.01

Appendix G. Instructions for Sample Collection, Processing, and Shipping Clinical Samples to the Cholinesterase Reference Lab (CRL) for Red Blood Cell Cholinesterase (RBC-ChE) Analysis

G-1. PURPOSE

To establish uniform specimen processing, shipping, and receiving procedures for RBC-ChE assays on clinical samples of nerve agent casualties.

G-2. DEFINITIONS

Buffy Coat - The layer of leukocytes that collect immediately above the red blood cells in sedimented or centrifuged whole blood.

Hemolyzed - Lysed (destroyed) red blood cells with the release of hemoglobin.

G-3. PROCEDURES

A. Specimen Collection. Specimens for cholinesterase analysis are collected in lavender-top EDTA vacutainers. All specimens will be labeled with the patient's full name, age, social security number, date and time specimen was drawn, and phlebotomist initials.

B. Specimen Processing and Handling

1. All specimens shall be centrifuged to ensure that the red blood cells (RBCs) have been separated from the plasma. **Separation must occur within four hours of specimen acquisition.** Any hemolyzed specimens must be discarded and redrawn. The plasma and the buffy coat are removed from the packed RBCs and discarded immediately after centrifugation. If the specimens cannot be analyzed and/or shipped immediately, they must be refrigerated at 2-8°C, and **not frozen (on arrival specimens must be 0-10°C).**

2. Units requesting primary RBC-ChE analysis by the CRL must ensure that specimens are received at CRL so that they can be assayed within 14 days of date drawn.

C. Specimen Shipping

1. Specimens shall be packed in an appropriately sized, insulated container with a sufficient number of ice packs to ensure the internal temperature of the shipping container is maintained at 2-8°C for the shipping period. Use the following guidelines for shipping RBC-ChE specimens:

(a) Layer bottom with appropriate number of ice packs, i.e., Polar Pack® or Super Ice® Re-usable freezer packs. **DO NOT USE DRY ICE TO SHIP SPECIMENS.** If ice packs are not available, use wet ice.

(b) Layer of packing material, i.e., absorbent pads or bubble plastic.

(c) Specimens

(d) Layer of packing material.

(e) Layer of appropriate number of ice packs.

(f) Repeat steps (b)-(e) until all specimens are packed.

(g) Fill in all dead space with appropriate amount of packing material.

2. Shipments of specimens to CRL, USACHPPM shall be scheduled to ensure that the specimens will arrive between 0830 hrs Monday and 1500 hrs Thursday. This scheduling is necessary to ensure that laboratory personnel will be present to accept the shipment and that the specimens will be properly stored. Questions concerning specimen shipping procedures should be directed to CRL, USACHPPM, at commercial **(410) 436-3983/2550 or DSN 584-3983/2550**. Specimens shall be sent to the following address:

Commander, USACHPPM
ATTN: MCHB-TS-LRD (Cholinesterase Laboratory)
Bldg. E-2100
Aberdeen Proving Ground, MD 21010-5403

D. Specimen Receipt and Processing

1. All shipments will be delivered directly to room 0200, building E2100.

2. All shipments will be unpacked the day of arrival. The Shipping Log will be noted with date and time of arrival, temperature of specimens, courier tracking number (if available), CRL shipment ID and technician's initials.

3. All shipments arriving at CRL, USACHPPM will meet the following criteria:

(a) All specimen tubes must be unopened and intact.

(b) No specimen will have a draw date greater than 14 days prior to receipt at CRL. If shipping times are greater than 5 days, notify in advance the CRL QA office.

(c) Plasma and buffy coat must be separated from the red blood cells prior to shipment.

(d) On arrival, specimen(s) must be at a temperature between 0-10°C.

(e) Properly labeled sample tubes and completed paperwork to include a master list of all specimens with patients' full names, social security numbers, ages, dates and times drawn, and times separated.

4. Failure to meet the above criteria will be cause for sample rejection and destruction. The sending facility will be notified and asked to redraw their specimens.

Appendix H. Incident Report Format for Suspected CW Exposure

Please enclose as much of the following information as possible. Transmit this information as soon as possible to USACHPPM at the contact information below. If shipping biomedical samples, also include this form (inserted inside of a plastic bag to protect from moisture) with the shipment.

US Army Center for Health Promotion and Preventive Medicine
ATTN: MCHB-TS-RDE
5158 Blackhawk Road
Aberdeen Proving Grounds, MD 21010-5422
1-800-222-9698, DSN 584-6096; or commercial (410) 436-6096
Secure DSN 584- or commercial 410-436-4244
Secure email: OEHdata@usachppm.smil.mil
*Secure web server:*usachppm1.army.smil.mil

Exposure Information:

Describe incident including date/time group, unit, and location of suspected exposure:

Onset date/time and description of clinical symptoms:

Sample collection date/time:

Potential CW agents involved:

Environmental sampling type, location, reading, and date/time:

Protective equipment in use at the time of the incident:

Patient Information:

Name / Rank:

Age / Gender / Social security number:

Unit / UIC:

CW agent-related casualty treatment:

Point of Contact Information:

Name:

Address:

Phone/Fax/E-mail: